

 The pervasive developmental disorders are early onset conditions characterized by delay and deviance in the development of social, communicative, and other skills.

 The onset of pervasive developmental disorders occurs during infancy, but the condition is usually not identified until the child is around three years old.

 Parents may begin to question the health of their child when developmental milestones are not met, including age appropriate motor movement and speech production.

 Children with PDD vary widely in abilities, intelligence, and behaviours.

 According to DSM-5, autism comes under the AUTISM SPECTRUM DISORDER and it is considered as a neurodevelopmental disorder.

ASD was previously known as PDD.

# Autistic Spectrum Disorders

Pervasive

Developmental

Disorder- Not

Otherwise Specified

(PDD-NOS)

Rett

Syndrome

Autism

Childhood

Disintegrative

Disorder

Asperger

Syndrome

Autistic disorder, also known as childhood autism, infantile
 autism, and early infantile autism, is, by far, the best known of
 the pervasive developmental disorders.

 Autistic disorder is characterized by impairments in three domains: social communication, restricted and repetitive behaviours, and aberrant language

## **HISTORY**

- In 1943 **LEO KANNER** described 11 cases of what he termed autistic disturbances of affective contact.
- In these cases, there was a congenital "inability to relate" to people in usual ways.
- Kanner also noted-
- -Unusual responses to the environment, both stereotyped motor mannerisms
- Resistance to change or insistence on sameness and pronoun reversal.



#### **HISTORY**

"Early infantile autism" was described by LEO KANNER in 1943.

• In 1867, the psychiatrist **HENRY MAUDSLEY** had observed a group of very young children with severe mental disorders characterized by marked deviation, delay, and distortion in development.

• In that era, most serious developmental disturbance in young children was believed to fall within the category of psychoses.

#### **HISTORY**

 In 1978 when MICHAEL RUTTER did subsequent research in a new definition that served, as the basis for that used in DSM-III.

 In DSM-III, the condition was first recognized and placed in a new class of disorders—the pervasive developmental disorders.



 In DSM-I & DSM-II, autism was not officially recognized; rather, it was viewed as being on some continuum with schizophrenia.



- In DSM-III-R, changes included-
  - -There was more attention to developmental concerns and a set of 16 very detailed criteria were provided.

-The multiaxial placement of autism and other PDD was done.

-The condition was moved to AXIS-II.

• In DSM-IV-TR, autism is defined on the basis of behavioural features and age of onset (age of onset must be before 3 years).

 Behavioural difficulties must include some feature of social disturbance, communicative disturbance, and restricted interests or repetitive behaviours.

• In ICD-9, the category of psychoses with onset in childhood included the subgroup of infantile autism, among others.

 The definitions of autism in both icd-10 and DSM-IV-TR are conceptually identical.

• In addition, the disorder was returned to AXIS-I.

#### **EPIDEMIOLOGY**

• VICTOR LOTTER- conducted the first epidemiological study of autism in 1966.

• Until the 1980s autism was considered to be a rare with prevalence of 4 per 10,000 children (fombonne,2005)

• The current prevalence estimated in us is 1%.

## **EPIDEMIOLOGY**

• According to CDC (center for disease control) - 1 in 500 to 1 in 166.

• In India-

- -Prevalence rate- 1 in 500 or 0.20%.
- -Incidence rate- 1 in 90,666

## **EPIDEMIOLOGY**

• Boys >girls, with ratios reported averaging around 3.5 or 4.0 to 1.

• Autism clearly is seen in all social classes and in all countries.

The onset of autism is almost always before age 3



• It includes-

- PSYCHOSOCIAL THEORIES
- BIOLOGICAL THEORIES
- IMMUNE THEORIES
- GENETIC FACTORS
- PERINATAL FACTORS
- NEUROANATOMICAL & NEUROCHEMICAL

#### **PSYCHOSOCIAL THEORIES-**

 Emotional factors might be involved in the pathogenesis of autism.

 The condition was always caused by the experience of a "REFRIGERATOR" mother who was not responsive to the child's emotional needs.

#### **BIOLOGICAL THEORIES-**

 As children with autism were followed, various factors suggested a biological basis of the condition.

 These included the high rates of mental retardation and seizure disorders and the recognition that various medical and genetic conditions were sometimes associated with autism.

 Although the underlying biological abnormalities of autism are unknown, efforts are now under way to delineate more precisely testable neuropathological mechanisms.

#### **IMMUNE THEORIES-**

 There has been a suggestion that maternal antibodies directed against the fetus may be produced in utero.

 There also have been reports of autism associated with viral infections.

 Considerable controversy has arisen over the question of whether exposure to the measles-mumps-rubella (MMR) immunization might be a causative factor.

 This assumption rests largely on case reports that link the apparent onset of autism with the immunization.

#### **GENETIC FACTORS-**

FAMILY AND TWIN STUDIES SHOWS-

-Up to 15% cases of ASD appear to be associated with a known genetic mutation, in most cases, its expression is dependent on multiple genes.

-First-degree relatives of affected individuals are 20- to 80-fold more likely to be affected.

- The concordance rate in two large twin studies was found to be-
  - 36% in monozygotic pairs vs 0% in dizygotic pairs and
  - 96% in monozygotic pairs vs 27% in dizygotic pairs.

• The heterogeneity in expression of symptoms suggests that there are multiple patterns of genetic expression.

- The critical role for synaptic formation and function was also considered after the recent specific findings regarding-
  - -NEUROLIGINS
  - -SHANK3
  - -CONTACTIN ASSOCIATED PROTEIN 2
  - -NEUREXIN 1
  - -THE FRAGILE X MENTAL RETARDATION 1 (FMR1) GENE

- The recent discovery of **copy number variation** has led to several important studies confirming the relevance of these types of changes.
- Variation in dna sequence is an also important aspect.
- The M-TOR, that is, mammalian target of rapamycin—linked synaptic plasticity mechanisms, which appear to be disrupted in ASD.

#### PERINATAL FACTORS-

- Many obstetric complications have been studied as possibly associated with autism.
- These include-
  - -PREMATURITY
  - -HYPOXIA
  - -BLEEDING DURING PREGNANCY
  - -CAESAREAN DELIVERY



-MATERNAL GESTATIONAL DIABETES

-MEDICATION USE (VALPROATE)

-BREECH PRESENTATION

-NEONATAL ENCEPHALOPATHY (NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE (NICE), 2011).

- It appears that individuals who were exposed to **thalidomide** prenatally were 50 times more likely to have a child with ASD than mothers in the general population (dufour-rainfray *et al., 2011*).
- *VPA*, an anti-epileptic drug, is another teratogen and has been shown to increase the prevalence among those exposed by 8–18 times compared to the general population (dufour-rainfray *et al.*, 2011).

 Four reviews (kolevzon et al., 2007; gardener et al., 2009; hultman et al., 2010; hamlyn et al., 2012) suggest that both advanced maternal and paternal age are risk factors for autism, with paternal age perhaps playing a more significant role.

#### **NEUROANATOMICAL & NEUROCHEMICAL-**

 There is good postmortem and neuroimaging evidence for abnormalities of the limbic system and circuitry within the temporal and frontal lobes.

 A significant decrease in the number of purkinje cells and granule cells in the cerebellum.

Brain Regions of Potential Importance in Autism	
BRAIN AREA	FUNCTIONS
Amygdala	Emotional arousal, emotion perception, and emotional learning
Extended amygdala, ventral striatum, and nucleus accumbens	Social reward circuitry
Fusiform gyrus (especially lateral aspect of the right fusiform)	Face (person) recognition Social cognition
	Interpreting higherical movement as a nonverbal communication

Interpreting biological movement as a nonverbal communication, Superior temporal sulcus including: Direction of eye gaze, facial expressions, hand, head,

and body gestures Superior temporal sulcus **Emotional learning** 

Lateral convexity of prefrontal

cortex

Medial prefrontal cortex Social cognition (interpreting what others might be thinking and feeling)

Mirror neuron network, action comprehension

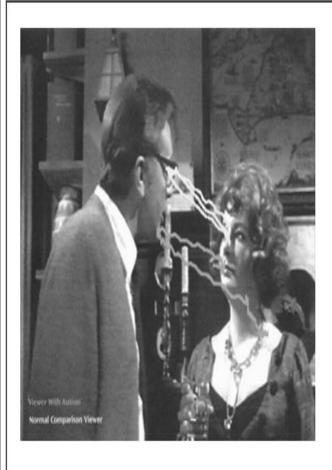
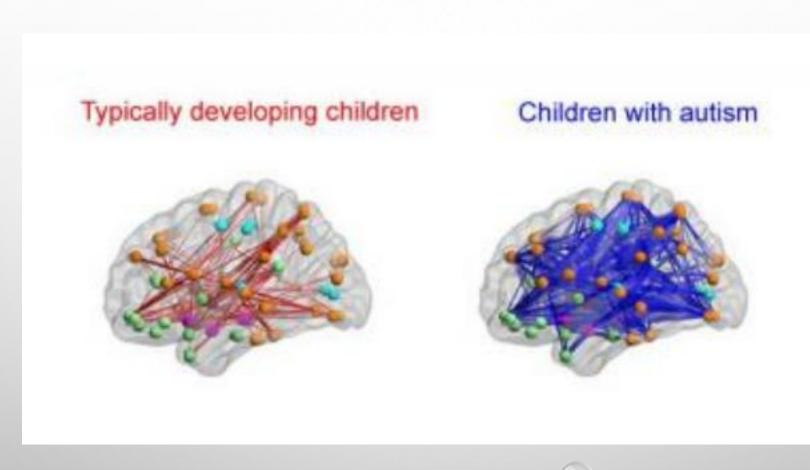


Figure 41-3. Eye tracking data from a typically developing young adult (top line) and a young, high-functioning man with autism (bottom line). The man with autism focuses almost exclusively on the mouth of the person speaking, avoiding the upper part of the face and not noticing the emotional responses of the listener. (From Klin A, Jones W, Schultz R: Defining and quantifying the social phenotype in autism. Am J Psychiatry. 2002;159:895, with permission.)

 There was decreased neuronal size, and increased neuronal packing density of neurons in the amygdala, hippocampus, septum, anterior cingulate, and mammillary bodies.

 The limbic system, especially the amygdala, is part of a neural system that supports social and emotional functioning and amygdala enlargement is seen in autism.





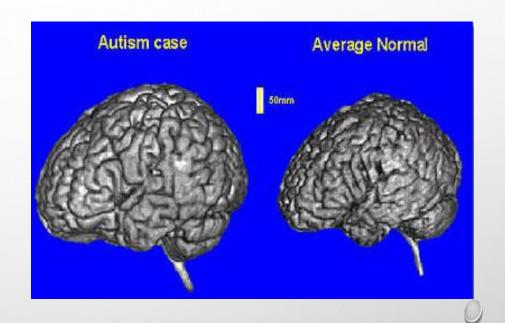
• Functional MRI (fMRI) has shown the amygdala to be hypoactive across a number of studies.

• The under activation of a region of the fusiform gyrus on the ventral surface of the temporal lobe during face perception tasks is seen in autism.



The overall brain size appears to be increased in autism.

(by 2 to 10%)



• The most consistent finding among neurotransmitters was that 25–50% of children and adolescents with autism have **elevated** serotonin levels in blood and platelets (mcdougle *et al., 2005; lamet al., 2006)* 

• A hyperdopaminergic functioning of the brain might explain the overactivity and stereotyped movements seen in autism.

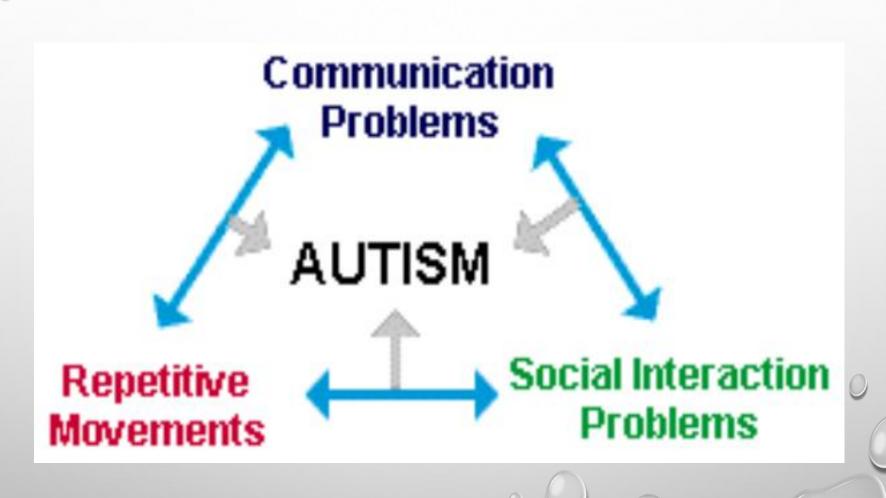
The endogenous opioids have been investigated, given the possibility that these compounds—enkephalins and endorphins—might lead to social withdrawal and unusual sensitivities to the environment.

• Moreover, **GABA abnormalities** in blood and platelets have been reported in individuals with autism (rolf *et al.*, 1993).

- Post mortem studies have identified widespread decreased number of GABA receptor binding sites (oblak et al., 2009).
- Fatemi et al. (2009) also suggest widespread decreases in expression of GABA synthetic enzymes and GABA receptors in a variety of brain region.

#### OTHER ETIOLOGIES-

- PHENYLKETONURIA
- NEUROFIBROMATOSIS
- CONGENITAL RUBELLA
- FRAGILE X SYNDROME
- TUBEROUS SCLEROSIS



#### A.CORE SYMPTOMS-

1. Persistent deficits in social communication and interaction

2.Qualitative impairment in verbal and nonverbal communication and play

3. Restricted, repetitive patterns of behaviour, interests and activities

#### 1. PERSISTENT DEFICITS IN SOCIAL COMMUNICATION AND INTERACTION-

- Do not conform to the expected level of reciprocal social skills and spontaneous nonverbal social interactions.
- Infants may not develop a social smile.
- And as older babies may lack the anticipatory posture for being picked up by a caretaker.
- Less frequent and poor eye contact.

 May not react as strongly to being left with a stranger compared to others their age.

• Children often feel and display extreme anxiety when their usual routine is disrupted.

• The social behaviour is often awkward and maybe inappropriate.

 In older school-aged children, social impairments may be manifested as-

- -A lack of conventional back and forth conversation
- -Fewer shared interests
- -Fewer body and facial gestures during conversations.

 Impaired ability to infer the feelings or emotional state of others around them.

 Have difficulty with making attributions about the motivation or intentions of others (also termed "theory of mind") and thus have difficulty developing empathy.



# 2.QUALITATIVE IMPAIRMENT IN VERBAL AND NONVERBAL COMMUNICATION AND PLAY-

• 30 to 40% of individuals with autism never use language for communication.

- Delays in the acquisition of language.
- There is no apparent motivation to engage in communication or attempt to communicate via nonverbal means.

May echo speech (echolalia).

 Have significant difficulty putting meaningful sentences together, even when they have large vocabularies.

 Use a word once and then not use it again for a week, a month, or years.

 In the 1st year of life, a typical pattern of babbling may be minimal or absent.

 Some children vocalize noises—clicks or nonsense syllables—in a stereotyped fashion, without a seeming intent of communication.

 The language patterns are frequently associated with pronoun reversals. For example- A child with autistic disorder might say, "you want the toy" when she means that she wants it.

• Difficulties in articulation are also common.

 Many children with autistic disorder use peculiar voice quality and rhythm.

3.RESTRICTED, REPETITIVE PATTERNS OF BEHAVIOUR, INTERESTS, AND ACTIVITIES-

- Developmentally expected exploratory play is restricted and muted.
- Toys and objects may not be used typically
- Instead, are often manipulated in a ritualistic manner, with fewer symbolic features.

- Do not show the level of imitative play that other children of their age exhibit spontaneously.
- The activities and play may appear more rigid, repetitive, and monotonous than their peers.
- Often seem to enjoy spinning, banging, and watching water flowing.
- May exhibit a strong attachment to a particular inanimate object.







**B.ASSOCIATED FEATURES-**

#### 1.ASSOCIATED PHYSICAL ANOMALIES-

- At first glance, they do not show any physical signs indicating the disorder.
- Overall, do exhibit higher rates of minor physical anomalies, such as ear malformations.
- Abnormal dermatoglyphics (E.G. Fingerprints)

2. IRRITABILITY- Includes aggression, self-injurious behaviours, and severe temper tantrums, temper outburts (meltdown)

3. INSTABILITY OF MOOD AND AFFECT- Sudden mood changes, with bursts of laughing crying without an obvious reason.

4. HYPERACTIVITY AND INATTENTION

#### 5.PRECOCIOUS SKILLS-

- Calculating abilities, usually beyond the capabilities of their normal peers
- Hyperlexia, an early ability to read well (even though they cannot understand what they read)
- Memorizing and reciting
- Musical abilities (singing or playing tunes or recognizing musical pieces).

6.INSOMNIA

7. INTELLECTUAL DISABILITY

8. MINOR INFECTIONS AND GASTROINTESTINAL SYMPTOMS

9.EATING PROBLEMS- May involve aversion to certain foods because of their texture, color, or smell, or insistence on eating a very limited choice of foods and refusal to try new.

#### 10. MOTOR AND SENSORY ABNORMALITIES-

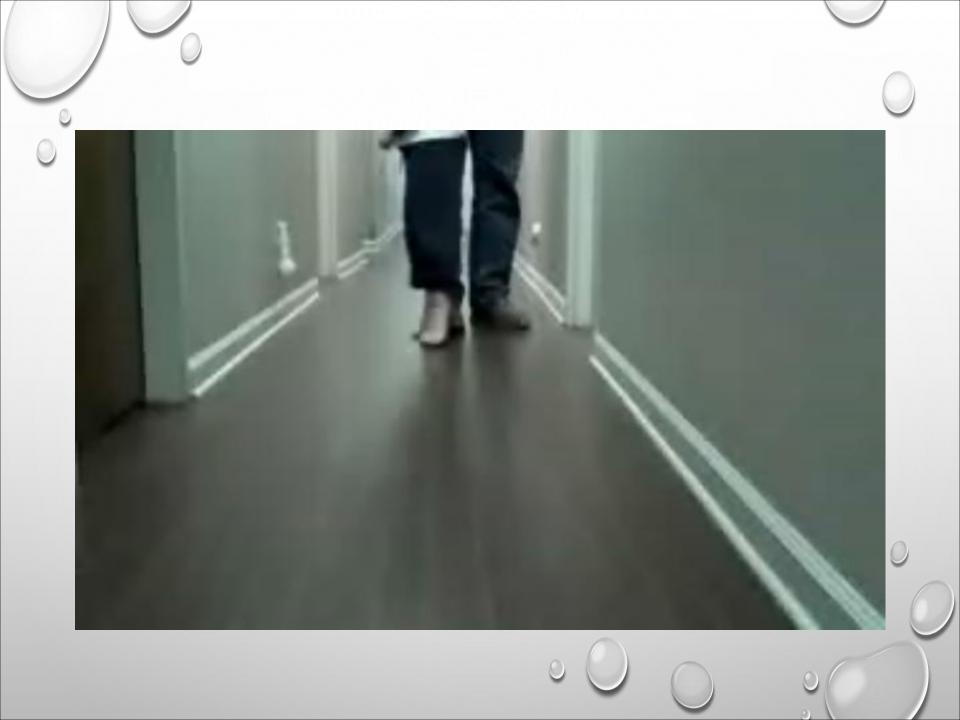
- Overrespond to some stimuli and underrespond to other sensory stimuli (e.G., To sound and pain).
- The child may appear deaf, at times showing little response to a normal speaking voice; on the other hand, the same child may show intent interest in the sound of a wristwatch.

- Do not respond to an injury by crying or seeking comfort.
- Some particularly enjoy spinning, swinging, and up-and-down movements.

- Toe walking can be seen in autistic child.
- Some children with autism may copy other people's motor movements (echopraxia).

 Bright lights may be distressing, although some autistic children are fascinated with light stimulation.

May be extreme sensitivity to touch (tactile defensiveness),
including major reactions to specific fabrics or affectional touch,
whereas there are many autistic children who appear insensitive
to pain and may not cry after a severe injury.





## PATHOLOGY & LAB EXAMINATION

TO RULE OUT ORGANICITY-

COMPLETE BLOOD INVESTIGATIONS

NEUROIMAGING

• EEG

#### PATHOLOGY & LAB EXAMINATION

#### • EEG-

- -The incidence of EEG abnormalities in autism- 10-83%
- -No abnormalities in the auditory brainstem pathways.
- -Abnormalities of cognitive potentials, particularly the auditory p300 (which represents the brain's processing of sensory stimuli), was shown in autism.

#### PATHOLOGY & LAB EXAMINATION

-It reflects abnormalities in higher auditory processing and neural pathways.

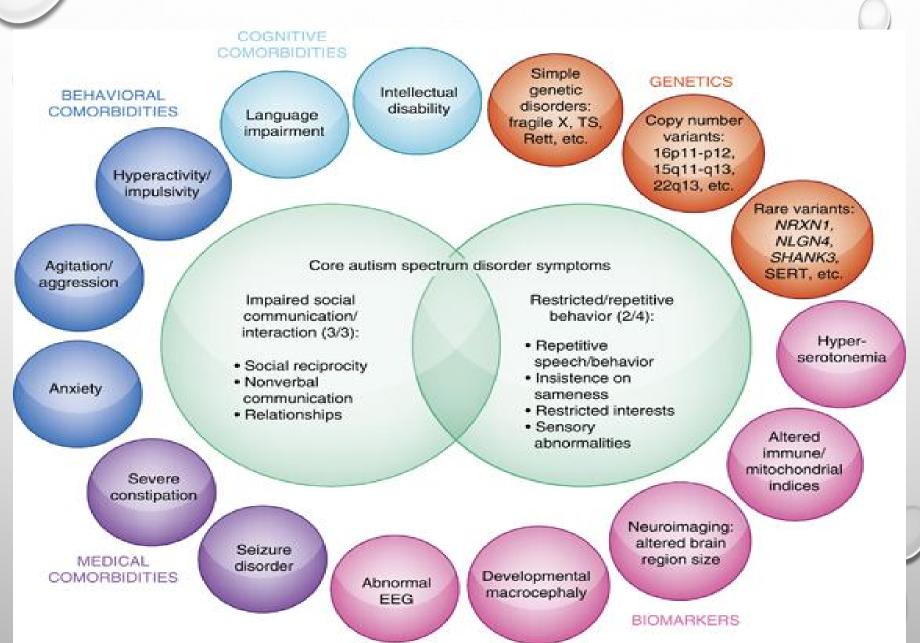
-Epilepsy in autism occurs in approximately 10-25% pts.

-Severe autistic individuals, that is lower-functioning individuals are at increased risk for epilepsy.



- CHILDHOOD AUTISM RATING SCALE (CARS)
- AUTISM DIAGNOSTIC OBSERVATION SCHEDULE (ADOS)
- AUTISM DIAGNOSTIC INTERVIEW-REVISED (ADI-R)
- AUTISM DIAGNOSTIC OBSERVATION SCHEDULE-GENERIC (ADOS-G)
- CHECKLIST FOR AUTISM IN TODDLERS (CHAT)
- SCREENING TOOL FOR AUTISM IN TWO YEAR OLDS (STAT)
- AUTISM BEHAVIOUR CHECKLIST (ABC)

#### COMORBIDITY



### DIFFERENTIAL DIAGNOSIS

 MICHAEL RUTTER AND LIONEL HERSOV suggested a stepwise approach to the D/D-

1. Social (pragmatic) communication disorder

2. Childhood onset schizophrenia

3. Intellectual disability with behavioural symptoms

Criteria	Autism Spectrum Disorder	Schizophrenia (with Onset before Puberty Rarely under 5 years of age	
Age of onset	Early developmental period		
Incidence	1 percent	<1 in 10,000	
Sex ratio (M:F)	4:1	1.67:1 (slight preponderance of males)	
Family history of schizophrenia	Not increased	Likely Increased	
Prenatal and perinatal complications	Increased	Not increased	
Behavioral characteristics	Poor social relatedness; may have aberrant language, speech or echolalia; stereotyped phrases; may have stereotypies, repetitive behaviors	Hallucinations and delusions; thought disorder	
Adaptive functioning	Impaired	Deterioration in functioning	
Level of intelligence	Wide range, may be intellectually disabled (30 percent)	Usually within normal range, may be low average normal	
Pattern of IQ	Typical higher performance than verbal	More even	
Grand mal seizures	4 percent to 32 percent	Low incidence	

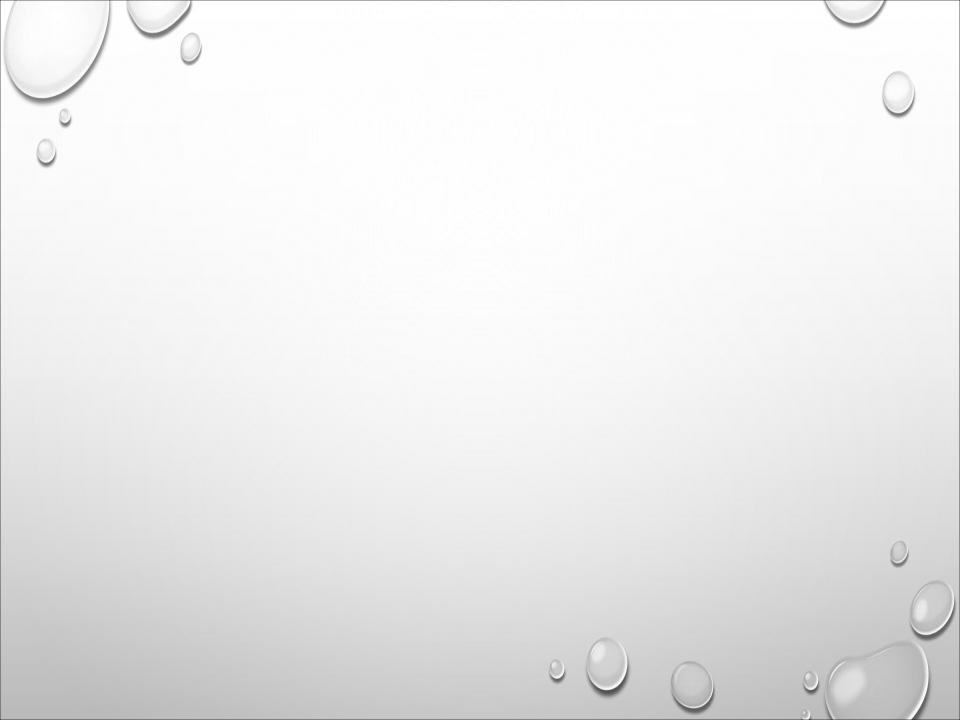
(Adapted from Magda Campbell, M.D., and Wayne Green, M.D.)

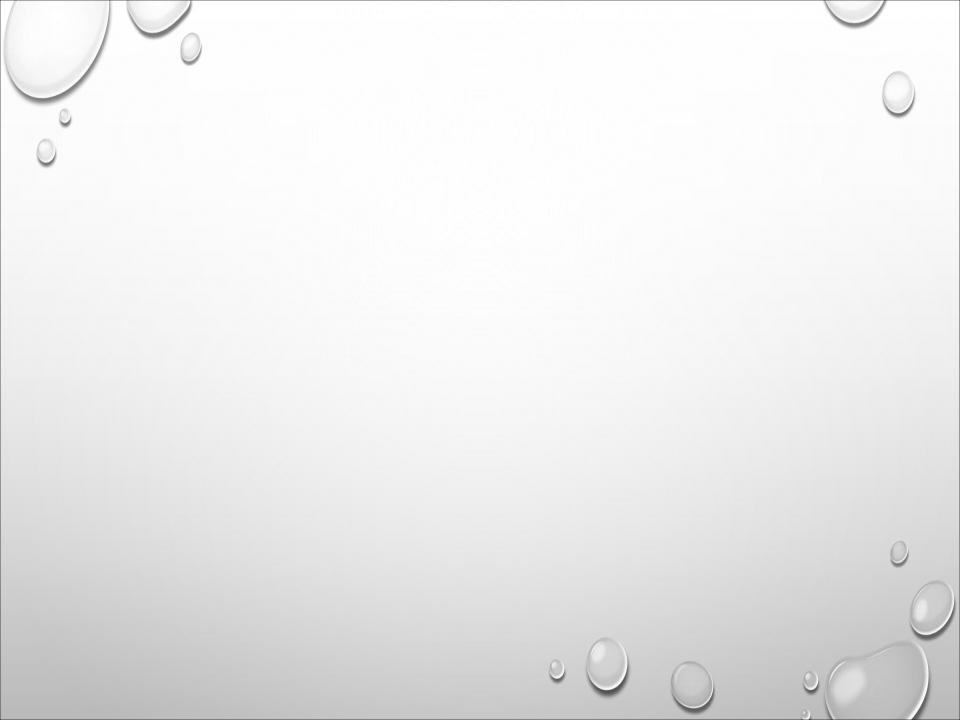
## DIFFERENTIAL DIAGNOSIS

4. Language disorder

5. Congenital deafness or hearing impairment

6. Psychosocial deprivation





Criteria	Autism Spectrum Disorder	Language Disorder	
Incidence	1 percent	5 of 10,000	
Sex ratio (M:F)	4:1	Equal or almost equal sex ratio	
Family history of speech delay or language problems	<25 percent of cases	25 percent of cases	
Associated deafness	Very infrequent	Not infrequent	
Nonverbal communication (e.g., gestures)	Impaired	Actively utilized	
Language abnormalities (e.g., echolalia, stereotyped phrases out of context)	Present in a subset	Uncommon	
Articulation problems	Infrequent	frequent	
Intellectual level	Impaired in a subset (about 30 percent)	Uncommon, less frequently severe	
Patterns of intelligence quotient (IQ) tests	Typically lower on verbal scores than performance scores;	Often verbal scores lower than performance scores	
Impaired social communication, restricted and repetitive behaviors,	Present	Absent or, if present, mild	
Imaginative play	Often impaired	Usually in tact	



NON AUTISTIC PDD-

-Asperger's syndrome

-Rett's syndrome

-Childhood disintegrative disorder

-Pervasive developmental disorder not otherwise specified

Table 41-4. Differential Diagnostic Features of Autism and Nonautistic Pervasive Developmental Disorders

Feature	Autistic Disorder	Asperger's Syndrome	Rett's Syndrome	Childhood Disintegrative Disorder	Pervasive Developmental Disorder Not Otherwise Specified
Age at recognition (mos)	0-36	Usually >36	5-30	>24	Variable
Sex ratio	Male > Female	Male ≫ Female	Female (rare Male)	Male > Female	Male > Female
Loss of skills	Variable	Usually not	Marked	Marked	Usually not
Social skills	Very poor	Poor	Varies with age	Very poor	Variable
Communication skills	Usually poor	Fair	Very poor	Very poor	Fair to good
Circumscribed interests	Variable (mechanical)	Marked (facts)	NA	NA	Variable
Family history—similar problems	Sometimes	Frequent	Not usually	No	Unknown

## COURSE & PROGNOSIS

 Autism is generally a lifelong disability, with most individuals needing significant family and community support.

 15 to 20% able to achieve independence and self-sufficiency in adulthood

## COURSE & PROGNOSIS

• Children with autism and IQs above 70 with average adaptive skills, who develop communicative language by ages 5 to 7 years, have the best prognoses.

• The prognosis of a given child with autism spectrum disorder is generally improved if the home environment is supportive.

## TREATMENT

The goals of treatment are to target core behaviours-

-To improve social interactions, communication, broaden strategies to integrate into schools

-Develop meaningful peer relationships

-Increase long-term skills in independent living

EARLY INTENSIVE BEHAVIOURAL & DEVELOPMENTAL INTERVENTIONS-

#### 1. UCLA/LOVAAS-BASED MODEL-

It is administered on a one-to-one basis for many hours per week.

A therapist and a child will work on practicing specific social skills, language
usage, and other target play skills, with reinforcement and rewards provided for
accomplishments and mastery of skills.

#### 2. EARLY START DENVER MODEL (ESDM) -

- Administered in naturalistic settings such as in day care, at home, and during play with other children.
- Parents are taught to be co-therapists and provide the training at home.
- The focus of the interventions is on developing basic play skills and relationship skills.
- It is applied within the context of the child's daily routine.

#### 3. PARENT TRAINING APPROACHES-

 Parents are taught to facilitate social and communication development within the home and during activities by targeting social behaviours.

SOCIAL SKILLS APPROACHES-

1.SOCIAL SKILLS TRAINING-

- Given guided practice in initiating social conversation, greetings, initiating games, and joint attention.
- Emotion identification and regulation, recognizing and learning how to label emotions in given social situations, learning to attribute appropriate emotional reactions in others, and social problemsolving techniques.

#### FOR REPETITIVE BEHAVIOURS & ASSOCIATED SYMPTOMS-

• 1.Behavioral interventions (BI)

• 2.Cognitive-behavioral therapy (CBT)

#### INTERVENTIONS FOR COMORBID SYMPTOMS-

1.NEUROFEEDBACK-by providing computer games or other games in which the desired behaviour is reinforced, while the child wears electrodes that monitor electrical activity in the brain.

2.INSOMNIA MANAGEMENT- Based on changing the parents behaviour toward the child at bedtime and throughout the night.

**EDUCATIONAL INTERVENTIONS-**

1. TREATMENT AND EDUCATION OF AUTISTIC AND COMMUNICATION-RELATED HANDICAPPED CHILDREN (TEACCH)-

- Originally developed at the university of north carolina at chapel hill in the 1970s
- TEACCH involves many visual supports and a picture schedule to aid in teaching academic subjects as well as socially appropriate responses.

#### 2. BROAD-BASED APPROACHES.

- These educational plans include a blend of teaching strategies and focus on language remediation.
- Behavioural reinforcement is provided for socially acceptable behaviours while academic subjects are being taught.
- TEACCH may also be incorporated.

#### 3. COMPUTER-BASED APPROACHES AND VIRTUAL REALITY-

- These are centered on using computer-based programs, games, and interactive programs to teach language acquisition and reading skills.
- The let's face it! Program is a computerized game that helps to teach children to recognize faces.
- It consists of seven interactive computer games that target changes in facial expression, attention to the eye region of the face, holistic face recognition, and identifying emotional expressions.

 No pharmacological agent has proven curative, but certain medications may be of benefit with regard to specific symptoms.

• Target symptoms include irritability, aggression, temper tantrums and self-injurious behaviours, hyperactivity, impulsivity, and inattention.

#### IRRITABILITY-

- Two SGA, risperidone and aripiprazole, have been approved by the FDA in the US for this.
- Dose of risperidone- 0.5mg to 1.5mg
- Risperidone has shown to be effective in aggressive or self-injurious behaviours.

- Aripiprazole has shown the treatment of tantrums, aggression, and self-injury.
- Doses ranged from 5 mg to 15 mg per day.
- Olanzapine has also been studied and found to be effective.

HYPERACTIVITY, IMPULSIVITY, AND INATTENTION-

Methylphenidate

Atomoxetine

Clonidine

#### REPETITIVE AND STEREOTYPIC BEHAVIOUR-

- SSRI antidepressants- fluoxetine, escitalopram
- SGAs-risperidone
- Mood-stabilizing agents- valproate

#### FOR BEHAVIOURAL IMPAIRMENT-

- Quetiapine- 50-200mg/day
- Clozapine- aggression and self-injurious behaviour coexist with psychotic symptoms.
- Ziprasidone, lithium, amantadine, clomipramine, tetrahydrobiopterin, venlafaine.



Music therapy

• Yoga

• Melatonin

• Vitamin c

Multivitamins

### CONCLUSION

 Autism is a type of neurodevelopmental disorder that comes under the ASD and ASD was previously known as PDD.

 Although progress has been made in measurement and diagnostic tools, in understanding prevalence and etiology and in developing evidence-based treatments both for core symptoms and comorbid conditions, much remains to be learned.

### CONCLUSION

- In terms of basic research, new paradigms are needed to uncover not only heterogeneous genetic mechanisms but also the functional impact of those genetic variants, including animal models and imaging studies.
- Finally, it is not known how best to disseminate training, knowledge, and the best practice about particular interventions among all professionals in contact with individuals with autism.

### CONCLUSION

 A key issue will be to identify early risk markers for ASD and cooccurring conditions that are amenable to interventions that could reduce the further difficulties with the inevitable adverse impacts on later lifetime functioning.

 Overall the ultimate goal is for a sufficiently accurate evidence base to inform effective intervention planning for every individual with autism and their family.



